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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/806,253	03/22/2004	David C. Baulcombe	4476-P02094US01	1920

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1601 MARKET STREET
SUITE 2400
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EXAMINER	
BOWMAN, AMY HUDSON	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/806,253	BAULCOMBE ET AL.	
	Examiner	Art Unit	
	Amy H. Bowman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-65* is/are pending in the application.

4a) Of the above claim(s) *33,34,42-46 and 50-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32,35-41 and 47-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/491,549.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/22/05, 11/18/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of group I, claims 32-41 and 47-49, as well as applicant's election of "mammal", in the reply filed on 6/26/2006 is acknowledged.

Applicant asserts that that groups I through V are drawn to closely related subject matter and therefore do not comprise separate and distinct inventions. Applicant further asserts that the examination of at least groups I-III together cannot be regarded as imposing a serious burden on the examiner. Applicant asserts that a proper search of group I would necessarily encompass a search of groups II and II as the methods encompassed by the claims result in detection of gene silencing.

Contrary to applicant's assertions, as explained in the office action mailed on 5/23/2006, each of the inventions are drawn to separate and distinct methods, each involving separate method steps and considerations that are not considerations of each of the other methods. The method of detecting a silenced gene in an organism, the process for isolating RNA molecules, and the method of determining the identity of a gene, of groups I-III, respectively, would each require a separate and distinct search and examination. These methods are not even classified in the same class and subclass, further demonstrating the necessity for a separate search and examination for each group.

The requirement for restriction is still deemed proper and is therefore made FINAL.

Claims 33, 34, 42-46, and 50-65 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no

allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 6/26/2006.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

In the instant case, the effective filing date of the instant claims is determined to be that of the instant application, 3/22/2004. These instant claims do not receive the benefit of the earlier filed priority documents because the documents do disclose the following limitations: characterizing any SRMs which are present in the extract such as to determine sequence identity or similarity with the target gene, as required by instant claim 32; preparing a library of genes from the organism and identifying those genes in the library which share sequence identity or similarity, with any SRMs which are present in the extract, as required by instant claim 41.

Furthermore, the priority documents do not disclose a limitation "21-25 nucleotides in length", as recited in instant claim 32; or "are between 23 and 25 nucleotides in length", as recited in instant claim 48.

Thus, the instant claims are accorded an effective filing date of 3/22/2004.

Specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). The specification does not support the following limitations that were added in the amended claims filed on 3/22/2004: characterizing any SRMs which are present in the extract such as to determine sequence identity or similarity with the target gene, as required by instant claim 32; preparing a library of genes from the organism and identifying those genes in the library which share sequence identity or similarity, with any SRMs which are present in the extract, as required by instant claim 41.

Furthermore, the specification does not support the limitation "21-25 nucleotides in length", as recited in instant claim 32; or "are between 23 and 25 nucleotides in length", as recited in instant claim 48. It is noted that the instant specification discloses support for a generic range wherein the SRMs are "approximately 25 nucleotides", but may be "slightly more or less than this characteristic length (say plus or minus 1, 2, 3, 4, or 5 nucleotides)" (see page 4 of the instant specification). However, the instant specification does not teach the specific ranges recited in instant claims 32 or 48.

There is no teaching in the instant specification that would lead one of ordinary skill to these specific ranges.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because:
> Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Specifically, there is a cross out on the date line under the signature of David Baulcombe that has not been initialed.

Additionally, this application presents a claim for subject matter not originally claimed or embraced in the statement of the invention. The oath is defective because although applicant is claiming the benefit of application 09/491,549 as a divisional, applicant has added subject matter in the amended claims filed on 3/22/2004 that is not supported by the parent applications, as explained in the "Priority" section above. Therefore, the instant application appears to be a continuation-in-part, rather than a divisional application and requires an oath that accounts for such.

A supplemental oath or declaration is required under 37 CFR 1.67. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

Claim Objections

Claims 32, 35-41 and 47-49 are objected to because of the following informalities: Claim 32 recites step (ii) twice. It appears that the second step (ii) is supposed to be step (iii). Appropriate correction is required.

Claim 32 recites, "(ii) analyzing said extract such as to determine the presence or absence of short RNA molecules which are 21-25 nucleotides in length (SRMs) in said extract". It appears that "(SRMs)" is located at the wrong position in the phrase since "(SRMs)" is not an abbreviation for "nucleotides in length". Appropriate correction is required.

Claims 35-41 and 47-49 are objected to because they depend from claim 32.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32, 35-41 and 47-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 32 recites, "(ii) analyzing said extract such as to determine the presence or absence of short RNA molecules which are 21-25 nucleotides in length (SRMs) in said extract". Steps iv and v of claim 32 assume the presence of SRMs, although according

to step ii of the claim, there may be an absence of SRMs. Therefore, steps iv and v are inoperable in the absence of SRMs.

Furthermore, step (v) of claim 32 recites, "correlating the presence of said SRMs". The metes and bounds of "correlating" cannot be determined. Applicant has not provided a definition. Claims 35-41 and 47-49 are rejected because they depend from claim 32.

Claim 41 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 41 is directed to the method of claim 32, further comprising "preparing a library of genes from said organism" and "identifying those genes in said library which share sequence identity or similarity, with any SRMs which are present in the extract as being genes which are silenced in the organism". Steps (vi) and (vii) of claim 41 are drawn to a library of genes, although the method of claim 32 is drawn to a method of detecting the silencing of a single target gene.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 32, 35-40 and 47-49 are rejected under 35 U.S.C. 102(b) as being anticipated by Agrawal et al. (WO 94/01550), as further evidenced by Bridge et al. (Nature Genetics, Vol. 34, No. 3, July 2003, pages 263-264).

The invention of the above claims is drawn to a method of detecting the silencing of a target gene in an organism comprising obtaining a sample of material and producing an extract from the sample, followed by analyzing the extract for the presence or absence of SRMs and gene silencing, wherein the organism is a mammal and the SRMs are antisense or sense RNA molecules. The silencing is associated with pathogen derived resistance and the target gene is a gene involved in apoptosis, a gene involved in cell-cycle regulation or a gene involved in a neurological process. The invention is further drawn to different sizes of SRMs.

Agrawal et al. teach improved self-stabilized oligonucleotides that are resistant to nucleolytic degradation that comprise two regions, a target hybridizing region having a sequence complementary to a nucleic acid sequence that is from a plant or animal virus, a pathogenic organism, or a cellular gene; and a self-complementary region having an oligonucleotide sequence complementary to a nucleic acid sequence that is within the self-stabilized oligonucleotide (see abstract). The self-stabilized oligonucleotides taught by Agrawal et al. therefore comprise a short antisense RNA molecule and a short sense RNA molecule, connected via a linker.

The oligonucleotides taught by Agrawal et al. are polymers of ribonucleotides or deoxyribonucleotides, and involve a self-complementary region of about 50 nucleotides or less (see page 15). The instant claim language recites that the short RNA molecules

"are" 21-25 nucleotides in length, "are" between 23 and 25 nucleotides in length, or "are" 25 nucleotides in length. It is noted that this language is interpreted as open language and therefore the molecules taught by Agrawal that comprise sense or antisense RNA molecules comprise RNA molecules that are 21-25 nucleotides in length, 23-25 nucleotides in length, or 25 nucleotides in length.

Agrawal et al. teach a method for inhibiting the gene expression of a virus comprising providing self-stabilized oligonucleotides or ribozymes to cells infected with the virus (see page 17). Agrawal et al. teach detection of target gene inhibition comprising testing oligonucleotides for their ability to inhibit HIV-1 in tissue culture (see example 3). Agrawal et al. teach introduction of the oligonucleotide, followed by production of a nucleic acid extract of the infected sample, and analyzing the extract for gene silencing. The extract taught by Agrawal et al. necessarily contained the short RNA molecules (the sense and antisense strands of the hairpin) that were inserted by the procedure.

As evidenced by the post-filing art of Bridge et al., short hairpin RNAs are processed to small interfering RNAs of 21 nucleotides that guide the cleavage of the cognate mRNA by the RNA-induced silencing complex (see abstract). Although Agrawal et al. are silent as to the processing of the hairpin structures into short sense and antisense RNAs, the hairpins taught by Agrawal et al. were necessarily cleaved into such fragments. As stated in the MPEP (see MPEP 2112), something that is old does not become patentable upon the discovery of a new property. The claiming of an unknown property which is inherently present in the prior art does not necessarily make

the claim patentable. There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of the invention, but only that the subject matter is in fact inherent in the prior art reference. Inherent anticipation does not require recognition in the prior art. Since Agrawal et al. teach formation and administration of double stranded hairpin RNAs of various sizes, and it has since been discovered that these hairpins are processed to short duplexes, the teachings of Agrawal et al. anticipate the instant invention. Furthermore, see *Eli Lilly & Co. v. Barr Labs., Inc., 251* F.3d 955, 970, 58 USPQ2d 1865 (Fed. Cir. 2001), "a limitation or the entire invention is inherent and in the public domain if it is the "natural result flowing from" the explicit disclosure of the prior art". This is considered to inherently anticipate the compound even though the compound's existence was not known.

Agrawal et al. teach a method of inhibiting the gene expression of a virus or a cellular gene comprising providing the self-stabilized oligonucleotides to cells (see page 17, for example). The cells were maintained under conditions in which degradation of the target mRNA occurred, thereby interfering with target RNA (see example 3, for example).

Additionally, as explained above, the hairpin structures taught by Agrawal et al. were necessarily cleaved into short sense and antisense RNAs, which would necessarily act through the instantly recited mechanisms of PTGS and co-suppression.

Therefore, the instant invention is anticipated by Agrawal et al., as further evidenced by Bridge et al.

Claims 32, 35, 36, 38, 40, and 47-49 are rejected under 35 U.S.C. 102(b) as being anticipated by Baracchini et al. (U.S. 5,801,154).

The invention of the above claims is drawn to a method of detecting the silencing of a target gene in an organism comprising obtaining a sample of material and producing an extract from the sample, followed by analyzing the extract for the presence or absence of SRMs and gene silencing, wherein the organism is a mammal and the SRMs are antisense RNA molecules. The target gene is a gene involved in apoptosis, a gene involved in cell-cycle regulation or a gene involved in a neurological process. The invention is further drawn to different sizes of SRMs. The instant claim language recites that the short RNA molecules "are" 21-25 nucleotides in length, "are" between 23 and 25 nucleotides in length, or "are" 25 nucleotides in length. It is noted that this language is interpreted as open language and therefore embraces larger fragments.

Baracchini et al. teach a method of inhibiting the expression of a target gene via interfering with target RNA comprising introducing an oligonucleotide having 8 to 30 nucleotides specifically hybridizable with a target nucleic acid that encodes MRP (see claim 26, for example). The oligonucleotides are for use in antisense inhibition of the function of RNA. Baracchini et al. teach that the oligonucleotides are oligomers or polymers of ribonucleic acid or deoxyribonucleic acid (see column 6). The oligonucleotide-treated cells can be cultured and screened for the desired result (see column 6).

Baracchini et al. teach detection of gene silencing followed by analyzing the extract for the presence or absence of the short RNA molecule and further teach experiments in nude mice. Baracchini et al. teach Northern blot analysis of the effects of oligonucleotides on MRP mRNA levels, wherein the oligonucleotides demonstrated to virtually eliminate target gene expression (see column 11).

Additionally, the oligonucleotides utilized in the method of Baracchini et al. meet the structural limitations of the instant claims and would therefore necessarily act through the instantly recited mechanisms of PTGS and co-suppression.

Therefore, the instant invention is anticipated by Baracchini et al.

Double Patenting Rejection

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 32, 36-41, 48 and 49 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7, 10 and 11 of U.S. Patent No. 6,753,139 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of Patent '139 are a species of the instantly recited claims. Specifically, the claims of Patent '139 and the claims of the instant application are each drawn to methods comprising the same steps except for the claims of Patent '139 specifically recite that the organism is a plant. Therefore, the claims of Patent '139 anticipate the instant claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy H. Bowman whose telephone number is 571-272-0755.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image

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